In the case herein reported, many of the clinical features of polyarteritis nodosa were present, and there was even biopsic evidence of the disease; yet some of the cardinal features were absent. At no time was renal, hepatic, splenic, or central and peripheral nervous system involvement observed. There is good reason to believe that the clinical episode of coronary arteritis with the associated peculiar, evanescent electrocardiographic changes was compatible with polyarteritis nodosa. Yet upon review of the electrocardiograms and considering the patient's clinical status at the corresponding times, it seems reasonable to believe that: (a) the cause was arteritis of a posteriorly located coronary branch, a counterpart of the arteritis observed in biopsy specimens; or, (b) that a tuberculous focus within the mediastinum adjacent to the pericardium and posterior wall of the heart could produce the same manifestations.

Wallgren[4] in Sweden observed that 70 per cent of cases of erythema nodosum in children were accompanied by evidence of active pulmonary disease, hilar changes as noted by x-ray, or other lesions, mainly of the lymphatic glands. In practically all the cases the disease was of the primary infection type. In the present case, the fact that the patient had a positive reaction to a tuberculin test in 1942 indicates that he must have had the primary infection years before the symptoms of the illness for which he was treated occurred. This is not at odds with the observation of the onset of erythema nodosum with recurrent exacerbations long after the time of initial infection, possibly as a result of secondary dissemination of the initial infection, or, conceivably, reinfection. Massini and Ramel[3] expressed the belief that recurrent erythema nodosum indicates a generalization of tuberculosis, tuberculous septicemia for example. Janussion,[3] on the other hand, felt that erythema nodosum is a sensitivity reaction—to primary tuberculosis in children, and to post-primary tuberculosis in adults. On the basis of Rich's[5] work it is known that resistance and sensitivity are two separate reactions on the part of the host to tubercle bacillus infection, and that the degrees of reaction do not necessarily correspond. The tuberculin skin test is based on hypersensitivity to the tubercle protein, and apparently in similar fashion erythema nodosum eruption arises as result of hematogenous spread of tubercle protein to hypergic skin. In the present case, of course, question arises as to why the reaction to the tuberculin skin test was but faintly positive during the acute phase of erythema nodosum eruption. The energy of overwhelming infection and minimal resistance is well known, but ordinarily a tuberculin skin test in the course of erythema nodosum due to tuberculosis causes exacerbation of the eruption. However, cases of erythema nodosum in which there were tuberculin-neutralizing properties in the serum have been reported.[2] Lofgren noted that the reaction to tuberculin was often stronger during the weeks following the acute eruption than while the lesions were present. Moreover he observed that in some cases there was no reaction or only faintly positive reaction to 0.0001 mg. of old tuberculin but pronounced positive reaction to 0.01 mg. of the substance. It does not seem too much to infer that perhaps the 0.00002 mg. of purified antigen contained in the purified protein derivative No. 1 used for skin testing in the present case was not a sufficient amount to evoke a highly positive reaction and exacerbation of the erythema nodosum eruption.

It is much easier to reconcile the biopsic observations with the outcome in the present case: Acid-fast organisms did not grow on cultures of material from the lesions and were not observed in stained specimens because the lesions were purely a hypersensitivity phenomenon secondary to tubercle protein and were not caused directly by viable organisms. Rich produced sterile hypersensitivity reactions in experimentally infected animals and also induced them by the injection of fractions of the tubercle bacillus. The presence of epithelioid and Langhans' giant cells, as well as the stromal involvement adjacent to the artery, in the case here reported might lead to suspicion that the condition was of granulomatous origin, but in the absence of bacilli and with the arteritic inflammatory changes more closely resembling those of involuting polyarteritis nodosa, the latter diagnosis was more credible.

SUMMARY

A case of tuberculous mediastinal lymphadenitis with erythema nodosum simulating polyarteritis nodosa is presented. An explanation is offered to reconcile the peculiar clinical manifestations on the basis of hypersensitivity, as well as to suggest that biopsy specimens of erythema nodosum may easily be confused with those of polyarteritis nodosa, a pleomorphic and generic entity.

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REFERENCES

1. Arkin, A.: A clinical and pathologic study of periarteritis nodosa, Am. J. Path., 6:401, 1930.

2. Kirby, P.: The etiology of erythema nodosum, British Journal of Radiology, 16:199, July 1943.

3. Lofgren, S.: Erythema Nodosum, P. A. Norstedt and Soner, Stockholm, 1946.

4. Miller, J. A., and Wallgren, A.: Pulmonary Tuberculosis in Adults and Children, Thos. Nelson & Sons, New York, 1939, pp. 126-130 and 153-154.

5. Rich, A. R.: The Pathogenesis of Tuberculosis, Chas. C. Thomas, Springfield, Ill., 1944. Chapters on hypersensitivity, the mechanism of hypersensitivity, application of the principles of pathogenesis.

Thrombocytopenic Purpura, Pregnancy and ACTH

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THROMBOCYTOPENIC PURPURA, although not common, has always caused great anxiety to obstetricians faced with the delivery of a patient with the disease and to surgeons contemplating splenectomy for such a patient.

In the past, massive blood transfusions and prayer have been the only answer to the problem. Recently, as the inherent dangers of transfusions have been better recognized, there has been a laudable search for techniques in which the use of blood and plasma is less important.

In this particular disease it seems that adrenocorticotropic hormone (ACTH) and cortisone will provide the answer. In the case of a woman with thrombocytopenic purpura who was at the full term of pregnancy, the drugs were used with dramatic effect before delivery and again before splenectomy.

REPORT OF A CASE

The patient, 36 years of age, gravida II, para I, was first observed July 11, 1951, with complaint of blood in the urine, first noted by her about one month previously in association with an attack of fever and aching diagnosed as "flu" by another physician. The hematuria had persisted and in addition the patient had noted rather severe bruising over her body, the presence of innumerable petechiae, especially below the waist, and excessive swelling of the legs. She stated, however, that in general she felt quite well.

The patient said that for years she had had eczema of the face and flexor surfaces of the arms and had used a coal tar preparation called "Zetar" for the past year. She had

also been taking an unknown quantity of thyroid substance for three years, three tablets of Theocalcin® daily for three years, and for the past several months a preparation containing iron and calcium. She had been told she had albuminuria at the time of her first pregnancy in 1947 and that intravenous pyelograms in 1948 were normal. The patient said that menstrual bleeding was not excessive, that bleeding from accidental wounds did not seem abnormal, and that there had been no unusual loss of blood at the time her first child was delivered. She had, however, always "bruised easily." She had had scarlet fever at age eight but no swelling or smoky urine subsequently.

The patient's grandfather had diabetes and her mother "bruised easily." None of five siblings had any bleeding tendency. One sibling had had infantile eczema; another had hay fever.

Upon physical examination, moderately severe eczematous changes of the face and arms were noted. There were many subcutaneous hemorrhages and innumerable petechiae, especially of the lower half of the body. Massive dependent edema to the level of the mid-thighs was present.

Reports on laboratory work on July 11, 1951, were as follows:

Blood: Hemoglobin content, 10.7 gm. per 100 cc.; packed cell volume, 35 per cent; platelets, 24,000 per cu. mm.; coagulation time, 11 minutes; bleeding time, over 18 minutes; clot retraction, none in five hours; prothrombin time, normal; leukocytes, 14,450 per cu. mm., made up of 78 per cent nonsegmented, 5 per cent segmented, 1 per cent eosinophils, 9 per cent lymphocytes, and 7 per cent monocytes. The urea nitrogen content was 11 mg. per 100 cc., the nonprotein nitrogen 28 mg. per 100 cc., and total serum proteins 5.0 mg. per 100 cc.

Urine: Specific gravity, 1.002; pH, 5.5; albumin, 4 plus. There was no sugar in the urine. In microscopic examination, innumerable erythrocytes were present.

The diagnosis was thrombocytopenic purpura, anemia due to loss of blood, glomerulonephritis in degenerative stage, dependent edema secondary to glomerulonephritis and aggravated by pregnancy.

The patient was admitted to hospital and was given 25 mg. of ACTH intramuscularly every six hours. The hematuria stopped and the blood-clotting mechanism reverted toward normal within 24 hours. On the sixth day the fetal sac was ruptured artificially and a 4 pound 8 ounce normal living female infant was delivered without abnormal bleeding either from the uterus or at the site of a small episiotomy. The dose of ACTH was reduced to a total of 50 mg. on the seventh day and to 25 mg. per day on the eighth day.

Results of studies of bone marrow obtained by puncture on the fourteenth and thirty-first days were identical. The hematologist reported: "Except for a slight shift to the left in the granulocyte series, both granulopoiesis and erythropoiesis were entirely normal. Megakaryocytes were abundant, many of them quite young. Many had a fine pinkish cytoplasmic granulation, but none had the normal, mature granulation of the platelet-producing megakaryocyte. Furthermore, very few were seen to be pinching off bits of their cytoplasm, and the few in which this phenomenon was seen were young forms, which were producing atypical granule-free masses of cytoplasm which could scarcely be characterized as platelets. Almost no normal platelets were seen on the smears. There was an abundance of eosinophils."

The patient was discharged on the fourteenth day with all medication proscribed in order to determine if the thrombopenia might be caused by any of the medicines previously used. On the thirtieth day she was again admitted to the hospital for splenectomy because of regression to the previous condition, with gross hematuria, massive bruising, innumerable petechiae, prolonged bleeding time, failure of clot retraction and worsening of the eczema, this time with petechial hemorrhages into the scales, causing startling raw-beef appearance. Cortisone was given, 25 mg. by mouth every four hours, and again there was a striking turn toward normal with respect to the bleeding tendency, and clearing of eczema, within 48 hours.

Splenectomy was carried out without incident on the thirty-fourth day. There was no unusual bleeding. The patient received 500 cc. of blood at the time of operation. She was given 75 mg. of ACTH intramuscularly the day before and the day after operation. Only "focal chronic inflammation, mild" was noted in biopsy of a specimen of muscle. "Chronic and acute passive hyperemia" was observed in pathologic examination of the spleen. The postoperative course was complicated by right lower lobe pneumonia which responded to the usual measures, and by severe recrudescence of eczema which gradually responded to local measures and x-ray therapy.

Dismissed from the hospital on the fiftieth day, the patient later was examined several times in the office. There was no recurrence of gross hematuria, but persistently there were 4 to 5 erythrocytes and equal numbers of oval fat bodies per high dry field, albumin content of 4 plus, and low specific gravity. When last observed December 19, 1951, the patient had no petechiae or bruises, but eczema still was present and there was moderate edema at the ankles. The number of platelets per cubic millimeter of blood was 150,000 and the clot retraction was normal. The lungs were quite clear. In repeated studies of the blood of the infant no abnormality was noted.

DISCUSSION

In any discussion of idiopathic thrombocytopenic purpura and its treatment, it must be borne in mind that many cases are acute and self-limited in a period of only a few days with or without treatment. It is to be noted also that ACTH and cortisone have not been effective in thrombocytopenic purpura when the marrow is hypoplastic or when there has been depression of platelet formation by chemical intoxication or medication.[3]

The fact that thrombocytopenic purpura responds to ACTH and cortisone raises the question as to the relation of this disease to asthma, eczema, polyarteritis nodosa and other diseases thought to be caused by allergic sensitivity and known to respond to these drugs.

Evans and co-workers[2] presented evidence for a common pathogenesis of primary thrombocytopenic purpura and acquired hemolytic anemia. Their evidence was not altogether direct, but they presented a reasonably convincing argument as to the close relationship of these two diseases, pointing out that there are patients with acquired hemolytic anemia and thrombocytopenia without purpura, another group with both acquired hemolytic anemia and thrombocytopenic purpura, and a third group with thrombocytopenic purpura and sensitized erythrocytes but no anemia. It has been possible with the Coombs test to demonstrate immunologic evidence of sensitization of the erythrocytes by an antibody active at 37° C., which is the evidence for the "allergic" basis of acquired hemolytic anemia. Similar attempts to demonstrate an anti-thrombocyte antibody in the serum of patients with thrombocytopenic purpura have been encouraging but not conclusive.

Furthermore, Bedson and Johnson[1] reported that the injection of an antithrombocyte serum into animals produced thrombocytopenic purpura and a proliferation of megakaryocytes in the bone marrow.

If there is a choice between ACTH and cortisone in the treatment of this condition, the author feels that cortisone

by mouth is better because it avoids the ecchymosis caused by the needle in the parenteral administration of ACTH.

While recognizing that in the present case the combination of eczema, renal abnormality and purpura suggested the diagnosis of one of the diseases of ground substance such as polyarteritis nodosa or lupus erythematosus, such a diagnosis was not warranted in view of the pathologic report on the muscle biopsy.

SUMMARY

A case of a patient at the full term of pregnancy who had glomerulonephritis in the degenerative stage, atopic eczema of the face and arms, and idiopathic thrombocytopenic purpura, is presented.

The bleeding tendency responded miraculously two times —once to ACTH, which made uneventful delivery of a normal infant possible, and the second time to cortisone, which made uneventful splenectomy possible. The nephrotic condition and eczema remained, but the bleeding tendency was still in remission eight months after splenectomy.

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REFERENCES

1. Bedson, S. P., and Johnson, M. E.: Further observations on platelet genesis, J. Path. & Bact., 28:101, 1925.

2. Evans, R. D.: Takahashi, K., Duane, R. T., Payne, R., and Liu, C. K.: Primary thrombocytopenic purpura and acquired hemolytic anemia: evidence for a common etiology, A.M.A. Arch. Int. Med., 87:48, Jan. 1951.

3. Mote, J. R.: Proceedings of the Second Clinical ACTH Conference, Vol. II, pages 173-180, 1951.

Interscapular Hibernoma—Report of a Case with a Brief Review of the Literature

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THE OCCURRENCE, in man,[2, 4, 7, 9, 10, 15] of peculiar lipomatous tumors featuring the presence of multiglobular fat, has occasionally been reported since Merkel,[11] in 1905, recorded the first instances. It was his belief that the growth was an adenoma of sebaceous glands. Gery,[7] however, in 1914, discussing a case reported by Bonnel,[2] called attention to the rather striking resemblance of the tumor, as microscopically observed, to the so-called hibernating gland of certain winter-sleeping mammals. Gery's suggestion that the term *hibernoma* be applied to these neoplasms was well received—and perhaps fortunately so. Although perhaps incorrectly implying that the neoplasm arose from some vestigial hibernating gland in the human species, the epithet *hibernoma* was so arresting that it led to special cataloguing in the literature.

In 1949 Brines and Johnson[4] published a detailed report of an interesting example of the condition and an excellent review of hibernomas. Ten cases (including one they reported) they listed as being authentic examples; seven others they did not consider sufficiently documented to warrant inclusion among the chosen few. Since the appearance of this review, Simon[15] has described a posterior cervical tumor of like nature and Kittle, Boley and Schafer[10] have reported a mediastinal tumor of this type. In both cases the tumor apparently was a hibernoma.

Special gross, microscopic and histochemical features of these tumors have been thoroughly discussed by the previously mentioned investigators, who, along with others,[1, 3, 5, 6, 12-14, 17] have dealt at length with the histogenesis of adipose tissue and its possible functions. Likewise, the relation of normal and tumorous fatty tissue to the so-called hibernating gland has been extensively investigated. Following is a report of a case of interscapular hibernoma, the thirteenth case of hibernoma to be recorded and the sixth in which the tumor originated at this site.

REPORT OF A CASE

A white housewife, 40 years of age, was admitted to the Hanford Sanitarium, Hanford, December 10, 1950, because of a large lump between the shoulder blades. The patient had first noticed the mass about ten or twelve years previously when it began to cause some discomfort when she was lying supine. Although it never had been painful, it had become more and more awkward to the patient as it gradually increased in size. Finally, in later years, development of the mass had made resting in a supine position impossible.

The patient was well-developed and well-nourished. The body weight was 130 pounds. On the posterior part of the upper portion of the thoracic wall between the scapulae was a mass so large and so deep in position that the peripheral borders of the scapulae overrode it. This was especially true of the right scapula, which when adducted became very prominent as it surmounted the growth. On palpation, the mass was freely movable beneath the skin and scapulae. It was rather firmer in consistency than the adjacent structures.

No abnormality was noted in examination of the blood or in urinalysis.

In view of the duration, size, shape, mobility, consistency, and position of the mass, it was thought to be a large lipoma. At operation the lesion was observed to be a large, firm, circumscribed, discoid, golden-yellow mass which was situated in the subcutaneous tissue. It had pushed the trapezius muscle aside in such a manner that the right margin of the muscle lay beneath the scapula. A lateral projection of the tumor extended into the axilla. Some portions of the attachments to adjacent tissues were very vascular. The tumor was removed completely except for the portion which had extended into the axilla. The operative wound was closed with little difficulty. The postoperative course was

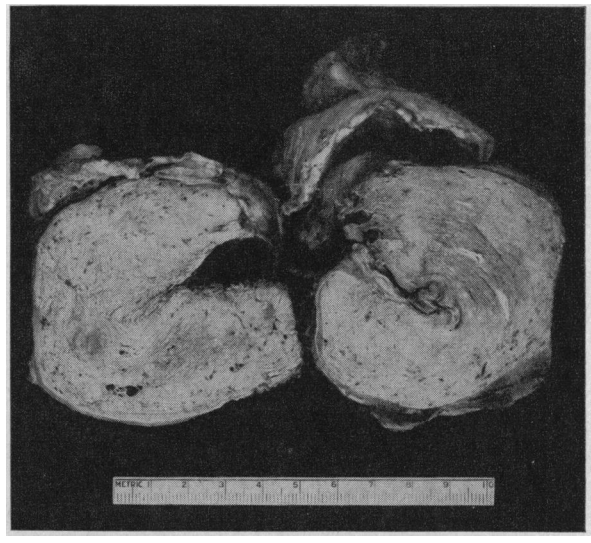

Figure 1.—Interscapular hibernoma. The cut surface is pale and fairly homogeneous, and encapsulation is apparent.